REMARKS

In response to the non-final Office action mailed March 16, 2009 from the PTO, favorable reconsideration is respectfully requested in view of the following remarks and claim amendment. Claims 1-24 are pending as of the mailing date of the instant Office action. Applicants acknowledge that claims 9, 10, 18 and 19 are currently under examination, and that all other claims are formally withdrawn from consideration. Claims 9-10 are amended without acquiescence in any rejection and without prejudice to the prosecution of any encompassed subject matter in a related divisional, continuation and/or continuation-in-part application. Applicants further wish to retain their rejoinder rights to all claims capable of rejoinder, and elect to defer making any required amendments until such time as the pending claims are acknowledged to be patentable.

Applicants have carefully considered the Examiner's remarks and the reference cited by the Examiner in conjunction with the instant Office action. The claim rejections, as set forth by the Examiner in the instant Office action, are herein addressed.

Claim Rejections under 35 U.S.C. § 102

Claims 9-10 and 18-19 remain rejected under 35 U.S.C. 102(b) as being anticipated by International Patent Application Publication No. WO 95/05819, hereinafter referred to as the "Lewy reference." Applicants respectfully traverse this ground of rejection.

As noted in response to the prior Office action, to anticipate the pending claims, the Lewy reference must teach each and every limitation of the claimed invention. Pending claim 9, as amended recites:

> Claim 9 (Currently amended): A method for achieving a circadian rhythm phase-delaying effect in a human, the method comprising the step of:
>
> administering to the human an amount of exogenous melatonin, melatonin agonist or compound that increases endogenous production of melatonin in the human,
> wherein said administration of the exogenous melatonin, melatonin agonist or compound produces in the human a level of plasma melatonin or ~~agonist concentration of greater melatonin or~~ equivalent agonist levels during the time interval from about CT 18 to about CT 6 ~~than from the time interval from about CT 6 to about CT 18~~, wherein

~~wherein~~ the plasma melatonin or equivalent agonist levels are elevated and maintained over the time interval from about CT 18 to about CT 6; or

the plasma melatonin or equivalent agonist levels are elevated and maintained during a time interval that overlaps about CT 0[[.]] and/or said administration of the exogenous melatonin, melatonin agonist or compound produces the plasma melatonin or equivalent agonist levels which are higher during the time interval from about CT 18 to about CT 6 than during the time interval from about CT 6 to about CT 18 to achieve an optimal phase-delaying effect.

Applicants respectfully request that the Examiner consider the amended claim with regard to the distinctions set forth herein as compared to the teachings of the Lewy reference. The instant invention teaches that the endogenous plasma melatonin or equivalent levels can remain elevated after CT 6 as long as they overlap about CT 0 and/or the levels are greater in the elevated time interval from about CT 18 to CT 6 than in the time interval from about CT 6 to CT 18. The Lewy reference did not have any teachings regarding a time interval or the duration within which the endogenous plasma melatonin or equivalent levels are elevated and maintained such as the time interval from about CT 18 to about CT 6 or a time interval that overlaps about CT 0.

Furthermore, in response to Applicants' arguments filed June 4, 2008, the Examiner asserts that "the instant claims do not require the elevation of physiological melatonin is *maintained* over a time interval that overlaps CT 0, but rather solely requires that the plasma melatonin or equivalent agonist levels are elevated *during a time interval that overlaps CT 0.*" (See page 7 of the Office action). The Examiner further asserts that:

> "Lewy et al. explicitly discloses that, for a phase delay, such as that which would be desired during travel to offset jet lag, the melatonin (or melatonin precursors, agonists, or compounds that mimic melatonin activity in place of melatonin itself) should be administered between CT12 and CT6, preferably between CT20 and CT2. Thus, the administration of melatonin (or its precursors, agonists, etc.) between CT20 and CT2 would clearly result in a higher melatonin concentration during this latter part of the circadian clock and also, notably, clearly falls within the range of CT18-CT6 as instantly claimed. Note again, as stated *supra,* that the instant claims do not require the greater plasma melatonin or agonist concentration to be *maintained* over the time interval from CT18 to CT6, but rather solely require that the plasma melatonin or equivalent agonist levels be

> greater during the time interval of CT18-CT6 than from the time interval from CT6-CT18, which is met by Lewy's teaching of melatonin (or its precursors, agonists, etc.) between the time interval of CT20-CT2." (See Page 8 of the Office action).
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> "As described *supra*, the instant claims do not recite any requirement that the plasma melatonin levels be *maintained* over the time interval of CT18-CT6 to result in a greater plasma melatonin concentration during this time interval, nor do they recite any requirement that the elevated plasma melatonin level be *maintained* over a time interval that overlaps CT0." (See Page 8 of the Office action).

While the Lewy reference focuses solely on administration times, the Lewy reference is limited to when elevated physiological melatonin concentrations began to rise. The Lewy reference contained no teachings about when the elevated physiological melatonin concentrations fell to normal levels. In contrast, the instant application focuses on the duration of the elevated plasma melatonin levels and when elevated physiological melatonin concentrations begin to fall to normal levels. Moreover, the instant application teaches that the plasma melatonin or equivalent agonist levels are elevated and maintained over the time interval from about CT 18 to about CT 6 or a time interval that overlaps about CT 0. The instant application teaches the importance of the time when elevated physiological melatonin levels begin to fall in order to determine phase delays in the time interval from about CT 18 to about CT 6 or a time interval that overlaps about CT 0.

The instant application discloses that the plasma melatonin or equivalent agonist levels are elevated and maintained over the time interval from about CT 18 to about CT 6 or a time interval that overlaps about CT 0 in the following:

> "For phase delays, exogenous melatonin administration produces in the human a plasma melatonin concentration of greater than quiescent melatonin levels for a time or in a concentration during a time interval from about CT 18 to about CT 6 that is greater than that produced during the time interval from about CT 6 to about CT 18." (See page 10-11, lines 28 to 1-3).
>
> "According to the methods of the invention, the duration of the exogenous melatonin pulse, as defined herein, is sufficient to overlap the endogenous melatonin offset time (typically, from CT 0 to CT 1) for any of these different types of administered formulations and preferably does not overlap the endogenous melatonin onset time." (See page 9, lines 22-25).

Applicants have amended the claims of the instant application to require that plasma melatonin or equivalent levels be elevated and maintained over the relevant time periods. The Lewy reference did not contain any teachings that the plasma melatonin or equivalent agonist levels are elevated and maintained over the time interval from about CT 18 to about CT 6 or a time interval that overlaps about CT 0. According to the Lewy reference, the administration of melatonin in the time interval from CT 20 to CT 2 does not result in plasma melatonin or equivalent agonist levels that are elevated and maintained over the time interval from about CT 18 to about CT 6 or a time interval that overlaps CT 0. The melatonin administration interval from CT 20 to CT 2 is not the duration within which the plasma melatonin or equivalent agonist levels are elevated and maintained.

The Lewy reference only taught that the exogenous melatonin can be administered at any time within the administration interval between CT 20 to CT 2 but without defining the duration of elevated and maintained levels. The instant application addresses for the first time the duration of elevated and maintained levels. By way of explanation, if the exogenous melatonin is administered at CT 20 and the duration of the administered melatonin is only three hours, the plasma melatonin or equivalent agonist levels will fall at CT 23 (one hour before CT 0) without the levels being elevated and maintained over a time interval that overlaps about CT 0 for an optimal phase-delaying effect. By way of another explanation, if the exogenous melatonin is administered at CT 2 and the duration of the exogenous melatonin is ten hours, the plasma melatonin or equivalent agonist levels start rising without the levels being elevated and maintained over the time interval that overlaps about CT 0 for an optimal phase-delaying effect. Furthermore, with a ten-hour duration starting at CT 2, the first four hours of elevated and maintained levels would fall within the correct time interval of CT 18 to CT 6; however, the latter six hours of elevated and maintained levels would be within the wrong time interval of CT 6 to CT 18. Therefore, the Lewy reference teaching and application does not result in plasma melatonin equivalent agonist levels which are higher during the time interval from about CT 18 to about CT 6 than during the time interval from about CT 6 to about CT 18 to achieve the optimal phase-delaying effect.

Consequently, the Lewy reference fails to teach that the plasma melatonin or equivalent agonist levels should be elevated and maintained during a time interval from about

CT 18 to about CT 6 such that they are greater during the time interval from about CT 18 to about CT 6 or that the levels are elevated and maintained over the time interval from about CT 18 to about CT 6 or a time interval that overlaps about CT 0 to achieve the optimal phase-delaying effect. The Lewy reference did not consider or anticipate that the duration of elevated and maintained levels might affect the optimal phase-delaying result.

Therefore, Applicants respectfully submit that the Lewy reference fails to anticipate the presently claimed invention that sets forth a new method for administering melatonin etc. to a human suffering from jet lag.

Accordingly, Applicants respectfully submit that claims 9-10 and 18-19 are allowable over the Lewy reference and reconsideration in view of the above amendment and remarks is requested. Applicants respectfully submit that the subject matter of the present claim is not anticipated by the Lewy reference under 35 U.S.C. § 102(b) and requests withdrawal of the rejection.

Judicially Created Doctrine of Obviousness-type Double Patenting

Claims 9-10 and 18-19 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 44-48 and 59 of U.S. Patent Application No. 10/945,843 and claims 1, 4-5, 9, 12-13 and 45 of U.S. Patent No. 5,591,768; or claims 1-3, 9, and 11 of U.S. Patent No. 5,716,978; or claims 1, 3-5, 7 and 9-10 of U.S. Patent No. 6,638,963; or claims 1-2 and 4 of U.S. Patent No. 6,794,407.

The Examiner asserts that:

> "A review of the original claims presented in the '382 application and those originally filed in the instant claims shows that the instant claims were not strictly commensurate in scope with those claims determined to be patentably distinct in the '382 application. For example, the instant claims recite several functions resulting from the administration of melatonin that were not pending in the original '382 claims (i.e., that the plasma melatonin or equivalent agonist levels are elevated during a time interval that overlaps CT0, or that the administration produces in the human a plasma melatonin or agonist concentration of greater melatonin or equivalent agonist levels during the time from about CT18 to about CT6 than from the time interval from about CT6 to about CT18). Furthermore, the claims of the '382 that are even closest (though not admitted by the Examiner to be identical to the instant claims) to the subject matter now claimed are also generic to a "phase-shifting" effect, and are not specific to the "phase-delay" as instantly claimed. Moreover, such claims of the

'382 also do not provide for the administration of the melatonin specifically after about CT18 and prior to about CT1." (See Pages 14-15 of the Office action).

"If Applicant has specific reasons for asserting that the rejection is improper, he is invited to clearly set such reasons forth on the record by analyzing the original claims filed and restricted in the '382 application and how they correspond to the claims originally filed in the instant application." (See Page 15 of the Office action).

"An obviousness-type double patenting rejection would be precluded if the instant claims filed in the instant application were filed as a result of the restriction requirement made in the '382 application and constituted one of the various patentably distinct but non-elected inventions of this '382 application." (See Page 15 of the Office action).

The Examiner has invited the Applicants to clearly set forth such reasons on the record for asserting that the obviousness-type double patenting rejection is improper by analyzing the original claims filed and restricted in the '382 application and how they correspond to the claims originally filed in the instant application.

The Restriction Requirement mailed June 9, 1999 for the '382 application restricted to one of the following inventions under 35 U.S.C. 121:

(I) Claims 1-11, 23-28, 47-74, 103, 104 and 109, drawn to methods for achieving a phase shift by administering melatonin or for administering melatonin without a phase shift;

(II) Claims 1-11, 23-38, 47-74, 103, 104 and 109, drawn to methods for achieving a phase shift by administering a melatonin agonist or for preventing said phase shift using the melatonin agonist;

(III) Claims 1-11, 23-28, 47-74, 103, 104 and 109, drawn to methods for achieving a phase shift by administering a compound that increases endogenous production of melatonin or of administering said compound without a phase shift;

(IV) Claims 12-22, drawn to methods for achieving a phase shift by administering a melatonin antagonist or of administering said antagonist without a phase shift;

(V) Claims 12-22, drawn to methods for achieving a phase shift by administering a melatonin inverse agonist or of administering said inverse agonist without a phase shift;

(VI) Claims 29-36, 75-88, 106 and 108, drawn to methods for achieving a phase shift by administering a compound which decreases the endogenous production of melatonin; or

(VII) Claims 37-46 and 89-102, drawn to methods of achieving a phase shift using light or of administering light without causing a phase shift.

In response to the Restriction Requirement mailed June 9, 1999 by the PTO in the '382 application, Applicants elected to prosecute Claims 1-11, 23-28, 47-74, 103, 104 and 109, designated as Group I by the Examiner and the species elected is melatonin with the result being a circadian rhythm phase shift. (See Response to Restriction Requirement for the '382 application dated June 28, 1999)

The Examiner further issued a Notice of Non-Responsive Amendment mailed March 1, 2000 for the '382 application requesting that Applicants specify whether a phase delay or a phase advance is produced rather than broadly claiming a phase shift for both the phase delay or the phase advance. In response to this Notice of Non-Responsive Amendment, Applicants specifically elected to prosecute the species of a phase advance. (See Supplemental Response to Restriction Requirement for the '382 application dated March 17, 2000).

Consequently, the species of a phase delay constituted one of the various patentably distinct but non-elected inventions of the '382 application.

Furthermore, Claim 25 of the '382 application claims "a method for achieving a circadian rhythm phase-shifting effect in a human an amount of melatonin, melatonin agonist or compound that increases endogenous production of melatonin in the human, wherein said administration produces in a human a plasma melatonin or agonist concentration of greater melatonin or equivalent agonist levels during the time interval from about CT 18 to about CT 6 than from the time interval from about CT 6 to about CT 18" which corresponds directly with Claim 9 of the instant application. Since the '382 application elected a phase advance, the instant application constitutes the species of a phase delay with the above-mentioned time intervals for the patentably distinct but non-elected inventions of the '382 application.

The Examiner asserts that "the '382 application does not provide for the administration of the melatonin specifically after about CT 18 and prior to about CT1." The '382 application includes such disclosure in the following:

> "In another embodiment, the invention provides a method for causing a circadian rhythm phase-shifting effect that is a phase delay, wherein the time of plasma melatonin concentration of greater than quiescent melatonin levels overlaps with the offset of endogenous melatonin production in the human. In a preferred embodiment, exogenous melatonin is administered to a human in an immediate-release formulation before about CT 1, preferably after about CT 18. Alternatively, exogenous melatonin is administered to a human in a delayed-release melatonin formulation at a time wherein plasma melatonin concentration in the human is increased to greater than quiescent levels before about CT 1 preferably after about CT 18." (See Column 6, Lines 23-35 of U.S. Patent No. 6,638,963 issued from the '382 application).

In the Notice of Non-Responsive Amendment mailed October 7, 1999, the PTO also required Applicants to specify administration of melatonin before about CT 1 or CT 14 but not both. In response to the Notice of Non-Responsive Amendment, Applicants specifically elected the administration time before about CT 14. (See Supplemental Response to Restriction Requirement dated December 7, 1999 for the '382 application.

Therefore, Applicants specifically elected to prosecute claims directed to administration of the melatonin before about CT 14 and not CT 1. Administration of the melatonin after about CT 18 and prior to about CT 1 constituted one of the various patentably distinct but non-elected inventions of the '382 application.

Furthermore, the '382 application electing the species of a phase advance has issued as U.S. Patent No. 6,638,963 by the PTO. The instant application is a divisional application of the '382 application. Applicants submit that the other patents recited as falling within the scope of the obviousness-type double patenting rejection are subject to the same distinctions Applicants set forth above with regard to the Lewy reference.

Based on the reasons stated above, Applicants respectfully request that the Examiner reconsider withdrawing the obviousness-type double patenting rejection because Applicants filed the instant application as a direct result of the restriction requirement made in the '382 application and because the original claims of the instant application directly correspond to the claims originally filed in the '382 application.

CONCLUSION

Reconsideration of the claims is respectfully requested in view of the above remarks. In the event that there are any questions concerning this response, or the application in general, the Examiner is respectfully urged to telephone the undersigned attorney so that prosecution of the application may be expedited.

A Petition for extension of time for three months is requested.

Please charge Deposit Account No. 13-3571 for any additional fees which may be required.

Respectfully submitted,

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